

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

ADA 017826

REPORT DOCUMENTATION PAGE		FEAD INSTRUCTIONS BEFORE COMPLETING FORM
1. REPORT NUMBER 14 SAM-TR-74-321	2. GOVT ACCESSION NO.	3. RECIPIENT'S CATALOG NUMBER 10
4. TITLE (and Subtitle) 6 HEART PATHOLOGY ASSOCIATED WITH EXPOSURE TO HIGH SUSTAINED +G _z		5. TYPE OF REPORT & PERIOD COVERED
7. AUTHOR(s) 10 R. R. Burton and W. F. MacKenzie		6. PERFORMING ORG. REPORT NUMBER
8. CONTRACT OR GRANT NUMBER(s)		10. PROGRAM ELEMENT, PROJECT, TASK AREA & WORK UNIT NUMBERS 17 793003 16 AF-7930
9. PERFORMING ORGANIZATION NAME AND ADDRESS USAFSAM School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas		12. REPORT DATE 25 Nov 74
11. CONTROLLING OFFICE NAME AND ADDRESS USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas		13. NUMBER OF PAGES
14. MONITORING AGENCY NAME & ADDRESS (if different from Controlling Office) 12 4 P. 11 1975		15. SECURITY CLASS. (of this report) UNCLASSIFIED
15a. DECLASSIFICATION/DOWNGRADING SCHEDULE		
16. DISTRIBUTION STATEMENT (of this Report) Approved for public release and sale; distribution unlimited.		
17. DISTRIBUTION STATEMENT (of the abstract entered in Block 20, if different from Report)		
18. SUPPLEMENTARY NOTES		
19. KEY WORDS (Continue on reverse side if necessary and identify by block number) Subendocardial hemorrhage Miniature swine Acceleration protection		
20. ABSTRACT (Continue on reverse side if necessary and identify by block number) The pathology of +G _z acceleration was examined using unanesthetized adult miniature and immature "farm-type" swine, with and without anti-G suit inflation. Following single exposures of +8 or 9 G _z for 45 to 90s--acceleration exposures that have been shown "tolerable" to man--swine were sacrificed and a detailed necropsy performed. Considering only the adult miniature swine, the endocardial area of the left ventricles showed evidence grossly of recent hemorrhage of varying severity involving both the wall and papillary muscles. The degree and		

DDC

RECEIVED
NOV 14 1975
C

DD FORM 1 JAN 73 1473

EDITION OF 1 NOV 65 IS OBSOLETE


UNCLASSIFIED

317000

UNCLASSIFIED

SECURITY CLASSIFICATION OF THIS PAGE (When Data Entered)

Location of the subendocardial hemorrhage was quantitated by grading the area of ventricle involved--1 (slight) to 4 (extensive). Of the 23 adult miniature pigs autopsied, the scores for papillary muscle hemorrhage, after 1 exposure to +9 G_z (45 to 90s) ranged from a mean of 2.3 to 3.3 and the extent of ventricular wall involvement was 2.5 to 3.3. Histologically, heart hemorrhage was limited to the subendocardial area, primarily involving the space between heart muscle and the endocardium and was particularly evident surrounding Purkinje fibers. Similar studies using immature farm-type swine (not miniature pigs) found these younger swine (4 to 5 months of age) to be less susceptible to such endocardial hemorrhage. Heart tissue recovery in these pigs following 1 exposure to +9 G_z for 45 s, required approximately 14 days. It appears that this lesion is similar although less severe than heart muscle lesions associated with low blood volume (hemorrhagic shock) studies and may have similar physiologic bases. It was concluded that particular attention should be made of the endocardium of victims of high performance aircraft accidents.



Joint Committee on Aviation Pathology:

II. Heart Pathology Associated With Exposure to High Sustained +G_z

R. R. BURTON and W. F. MACKENZIE

USAF School of Aerospace Medicine, Brooks Air Force Base,
Texas 78235

BURTON, R. R., and W. F. MACKENZIE. *Joint Committee on Aviation Pathology: II. Heart pathology associated with exposure to high sustained +G_z*. *Aviat. Space Environ. Med.* 46(10):1251-1253, 1975.

The pathology of +G_z acceleration was examined using unanesthetized adult miniature and immature "farm-type" swine, with and without anti-G suit inflation. Following single exposures of +8 or 9 G_z for 45 to 90 s—acceleration exposures that have been shown "tolerable" to man—swine were sacrificed and a detailed necropsy performed. Considering only the adult miniature swine, the endocardial area of the left ventricles showed evidence grossly of recent hemorrhage of varying severity involving both the wall and papillary muscles. The degree and location of the subendocardial hemorrhage were quantitated by grading the area of ventricle involved—1 (slight) to 4 (extensive). Of the 23 adult miniature pigs autopsied, the scores for papillary muscle hemorrhage, after one exposure to +9 G_z (45 to 90 s) ranged from a mean of 2.3 to 3.3 and the extent of ventricular wall involvement was 2.5 to 3.3. Histologically, heart hemorrhage was limited to the subendocardial area, primarily involving the space between heart muscle and the endocardium and was particularly evident surrounding Purkinje's fibers. Similar studies using immature farm-type swine (not miniature pigs) found these younger swine (4 to 5 months of age) to be less susceptible to such endocardial hemorrhage. Heart tissue recovery in these pigs following one exposure to +9 G_z for 45 s, required approximately 14 d. It appears that this lesion is similar, although less severe, than heart muscle lesions associated with low blood volume (hemorrhagic shock) studies and may have similar physiologic bases. It was concluded that particular attention should be made of the endocardium of victims of high-performance aircraft accidents.

MODERN fighter aircraft are capable of developing high sustained accelerations; i.e., acceleration levels of 6 G and above for durations longer than 15 s. Man wearing an anti-G suit and performing a straining maneuver (M-1 or L-1) has tolerated +9 G_z for 45 s and +8 G_z for 60 s without loss of vision (4,6). This is a significant increase in human tolerance to +G_z over previously published reports; i.e., a new accelerative environment tolerable to man has been identified which has been termed high sustained G (HSG) (2).

Since "protective" methods against G are not available—anti-G devices only increase G tolerance (the ability of man to endure G) in combination with physical exertion

—it is conceivable that man is exposing himself to an altered environment that "may be hazardous to his health."

The possibility that HSG may produce pathology in an animal that physiologically responds to G similarly to man was examined using swine—both immature "farm-type" swine and adult miniature pigs. The unanesthetized pig, especially adult miniature swine, was chosen because it has been found to be an acceptable human-analog for pathophysiology studies of +G_z (1).

Accordingly, several unanesthetized female swine were exposed to various levels, durations, and conditions of HSG, after which they were euthanized and gross and microscopic pathology performed. The results of these HSG pathology studies are reported herein.

MATERIALS AND METHODS

Swine were exposed to various accelerations using the "animal end" of the human centrifuge at the School of Aerospace Medicine (SAM), Brooks AFB, Tx. Methods used in exposing unanesthetized swine to acceleration, including anti-G suit application, have been described in a previous report (1). Acceleration exposure levels, durations, and conditions will be indicated in the "results" section as appropriate.

Immediately after the final acceleration exposure the pig was euthanized with an overdose of i.v. pentobarbital. The thoracic cage was opened, the heart removed, gross pathology determined, and tissues immediately harvested for histopathology.

RESULTS

Gross Pathology: The only consistent pathologies observed grossly in both adult miniature and farm-type immature swine following HSG exposures were hemorrhage of the skeletal muscles of the rear leg (particularly in the thigh region) and subendocardial hemorrhage of the left ventricle. The right ventricle was less often in-

The research reported in this paper was conducted by personnel of the Environmental Sciences Division and Veterinary Sciences Division, USAF School of Aerospace Medicine.

*The animals involved in this study were maintained and used in accordance with the Animal Welfare Act of 1970 and the "Guide for the Care and Use of Laboratory Animals" prepared by the National Academy of Sciences—National Research Council.



Fig. 1. The endocardial wall of the left ventricle of an adult miniature swine after exposure to HSG. The black areas involving particularly the papillary muscles are evidence of recent subendocardial hemorrhage (grade 4).

involved. The ventricular hemorrhage involved specifically both the papillary muscle and the muscular ridges, which are prominent in the heart of the pig and run parallel and longitudinally over the entire left ventricle below the origin of the cardiac valves. The papillary muscle showed hemorrhage beginning at the insertion of the chordae tendineae and extending down the papillary muscle onto the ventricular wall (Fig. 1).

In order to quantify the degree of ventricular hemorrhage found in each heart, a scoring system of 1 to 4 was devised, the number increasing with the increasing severity of hemorrhage. A score (grade) of 1 indicated a slight hemorrhage, barely visible, and involving only one area of no more than 1 cm². A grade of 4 was rarely used and indicated the occurrence of the most severe ventricular hemorrhage involving several areas of wall and papillary muscle and each site usually several cm² in area. Never did the endocardial tissue rupture and allow bleeding into the ventricular cavity. The heart hemorrhage shown in Fig. 1 involved the papillary and wall subendocardium and was graded 4.

Incidence of Subendocardial Hemorrhage: The results from 23 adult miniature swine, 30 to 55 kg body mass, exposed to various levels and durations of HSG (grouped accordingly) regarding the incidence of cardiac hemorrhage are shown in Table 1.

It is not difficult to produce minor, grade 1, subendocardial hemorrhage in the left ventricle of adult miniature swine (groups 7-10); however, the more severe lesions are restricted to exposures of high G levels for long durations (groups 1-3, 6).

Duration of exposure appears to be an important consideration regarding heart hemorrhage; e.g., pathology was more severe after exposure to 8 G for 45 s in group 6 than 9 G for 15 s in group 5.

The use of the anti-G suit appears to reduce the severity of the heart lesions but does not prevent the occurrence of pathology—9-G exposures for 90 s without the

TABLE 1. INCIDENCE AND SEVERITY* OF SUBENDOCARDIAL HEMORRHAGE OF ADULT MINIATURE SWINE AFTER EXPOSURE TO VARIOUS LEVELS AND DURATIONS OF +G_z.

Group	Level	+G _z ¹ Duration (seconds)	Anti-G Suit	N ²	Hem. Grade* Left Ventricle	
					Papillary	Wall
1	9	90	No	3	3.3	3.3
2	9	90	Yes	1	3	3
3	9	45	Yes	6	2.3	2.5
4	9	45 ³	Yes	2	0.0	0.0
5	9	15	Yes	2	0.5	0.5
6	8	45	Yes	2	1.5	2.0
7	8	15	Yes	2	1.0	1.0
8	7	15	Yes	1	0.0	1.0
9	5	45	Yes	1	0.0	1.0
10	5	15	Yes	1	0.0	2.0
11	0.3	45	No	2	0.0	0.0

*See text regarding methods of quantifying the severity of hemorrhage.

¹preceded by lower +G_z exposures of 3, 5, and/or 7 G for 15 to 45 s each (except for 0.3-G control runs).

²number of animals per group.

³repeated biweekly for 15 exposures.

anti-G suit frequently produced lesions that were unusually severe (grade 4).

Two swine were exposed to HSG biweekly for a total of 15 exposures (group 4, Table 1). Quite unexpectedly, these animals did not exhibit ventricular hemorrhage on gross examination. However on microscopic examination the presence of hemosiderin suggested evidence of previous hemorrhage. This suggests that repeated exposure to HSG may provide some type of anatomic or physiologic "adaptation" to this environment.

This study was extended using immature farm-type swine 5 to 6 months of age. This type of pig was considered because it was less expensive to buy, could be purchased locally, and an adequate supply was available. Although 56 of these pigs were employed, several factors were involved in eventually discontinuing their use. The primary considerations were age and body size. Interestingly, a pig under 5 months of age does not exhibit heart hemorrhage after exposure to HSG. However, older pigs are susceptible to subendocardial hemorrhage, almost to the same degree as an adult miniature swine; yet, at this age it frequently is too large to effectively restrain without anesthesia. Also, since this study was applicable to HSG exposures of adult man, the variables associated with body growth of an immature animal model were considered to be significant but incalculable.

The results of the study of subendocardial hemorrhage in which 56 immature swine were exposed to HSG are summarized as follows: a) extremely young animals do not exhibit subendocardial hemorrhage after HSG exposure; b) the anti-G suit reduces the severity of the heart lesions as suggested in the adult swine study; c) increasing oxygen (70 to 80% of the breathing mixture of the pig) or decreasing oxygen (12 to 14% of the breathing mixture) in combination with HSG exposure does not alter the severity of the subendocardial lesions expected of HSG exposure alone; and, d) after one exposure of HSG, it requires approximately 2 weeks for the sub-

TABLE II. INCIDENCE AND DEGREE OF SUBENDOCARDIAL HEMORRHAGE OF THE LEFT VENTRICLE IN IMMATURE SWINE FOLLOWING EXPOSURE TO 45 S OF +9 G_z WITHOUT THE ANTI-G SUIT.

Days after Exposure to HSG	N*	Hemorrhage Score	
		Papillary	Wall
0	5	3	2.6
3	3	3.3	3.3
7	3	1	1
14	3	0	0

*N = number of pigs per group.

endocardial hemorrhage to disappear on gross examination (Table II).

Histopathology of Subendocardial Hemorrhage: Histologically, areas of multifocal subendocardial hemorrhages were noted which were usually confined to the subendocardial tissue, although occasionally they were found deeper in the myocardium, but never greater than 1 or 2 mm in depth. Frequently, Purkinje's fibers, which are numerous in this area, were completely surrounded by hemorrhage. There was no significant inflammatory response observed in the tissue of the myocardium or endocardium, except for occasional isolated neutrophils or lymphocytes, which were extravasated from the vessels. This was expected since the interval between stress and death was inadequate to allow for an inflammatory response and eliminates all previous cardiopathies. An example of the histologic appearance of subendocardial hemorrhage is shown at right in Fig. 2. Histopathology of subendocardial hemorrhage was not different between immature farm-type pigs and mature miniature swine. Patchy multifocal microscopic areas of myocardial degeneration also occurred in areas of hemorrhage.

DISCUSSION

Heart pathology (subendocardial hemorrhage) has been produced in swine wearing anti-G suits by exposure to HSG. The acceleration levels used were not extreme but of the magnitude previously experienced by man (4,6). Of particular importance is the involvement of Purkinje's fibers and possible interference with the conductive properties of the heart—the development of serious cardiac arrhythmias.

Subendocardial hemorrhage similar to our findings has been reported in several species of animals, including the pig, after they had experienced 1 to 3 h of severe hemorrhagic shock (3). However, in addition to subendocardial hemorrhage, they reported more severe cardiac pathologies than we were able to detect; e.g., myocardial necrosis and "zonal lesions." Martin *et al.* (5) concluded that, in order to get heart pathologies of this nature, it required tachycardia, decreased ventricular volumes, and an increased positive inotropic response—all of which occur during exposure to HSG. The major difference between HSG and hemorrhagic shock appears to be the duration of exposure; viz HSG lasts for a maximum of only 90 s (in our study) whereas hemorrhagic shock experiments are of at least 1 h duration. Presumably therefore, the endocardial lesions associated with HSG may well be only the initial lesions of the



Fig. 2. Top: H and E stain $\times 76$ of section of normal ventricular wall in the region of the endocardium. Bottom: H and E stain $\times 76$ of section of ventricular wall showing subendocardial hemorrhage.

more severe myocardial necrosis associated with hemorrhagic shock.

REFERENCES

1. Burton, R. R. 1973. Positive (+G_z) acceleration tolerances of the miniature swine: Application as a human analog. *Aerospace Med.* 44:294-298.
2. Burton, R. R., S. D. Leverett, Jr., and E. D. Michaelson. 1974. Man at high sustained +G_z acceleration: A review. *Aerospace Med.* 45:1115-1136.
3. Chang, J., and D. B. Hackel. 1973. Comparative study of myocardial lesions in hemorrhagic shock. *Lab. Invest.* 28:641-647.
4. Leverett, S. D., Jr., R. R. Burton, R. J. Crossley, E. D. Michaelson, and S. J. Shubrooks, Jr. 1973. Physiologic responses to high sustained +G_z acceleration. USAF-SAM-TR-73-21.
5. Martin, A. M., D. B. Hackel, M. L. Entman, M. P. Capp, and M. S. Spach. 1969. Mechanisms in the development of myocardial lesions in hemorrhagic shock. *Ann. N. Y. Acad. Sci.* 156:79-90.
6. Parkhurst, M. J., S. D. Leverett, Jr., and S. J. Shubrooks, Jr. 1972. Human tolerance to high, sustained +G_z acceleration. *Aerospace Med.* 43:708-712.